

CLAIMS

Sub C1 1. A method for production of an autologous vaccine to tumor cells comprising transducing the tumor cells with one or more species herpes simplex virus amplicon containing the gene for an immunomodulatory protein and at least one additional therapeutic gene to provide transient expression of the immunomodulatory protein and the therapeutic gene product by the cells.

2. The method according to claim 1, wherein the tumor cells are transduced with the herpes simplex amplicons *ex vivo*.

3. The method according to claim 1, wherein the tumor cells are transduced with the herpes simplex cell *in vivo*.

4. A method for inducing a protective immune response to tumor cells in a patient comprising the step of transducing the tumor cells with one or more species herpes simplex virus amplicon containing the gene for an immunomodulatory protein and at least one additional therapeutic gene to provide transient expression of the immunomodulatory protein and the therapeutic gene product by the cells.

5. The method according to claim 4, wherein the tumor cells are transduced with the amplicon *ex vivo*, further comprising the step of introducing the transduced tumor cells into the patient.

6. The method according to claim 4, wherein the amplicons are injected into the site of the tumor cells *in vivo*.

7. The method according to any of claims 1 to 6, wherein the immunomodulatory protein is a cytokine.

8. The method according to claim 7, wherein the cytokine is interleukin-2

1 9. The method according to claim 7, wherein the cytokine is granulocyte-
2 macrophage colony stimulating factor.

1 10. The method according to claim 7, wherein the immunomodulatory
2 protein is a chemokine.

1 11. The method according to claim 10, wherein the chemokine is
2 RANTES.

1 12. The method according to ~~any of claims~~ claim 1 to 6, wherein the
2 immunomodulatory protein is a intercellular adhesion molecule.

1 13. The method according to claim 12, wherein the intracellular adhesion
2 molecule is ICAM-1.

1 14. The method according to ~~any of claims~~ 1 to 6, wherein the
2 immunomodulatory protein is a costimulatory factor.

1 15. The method according to claim 14, wherein the costimulatory factor
2 is B7.1.

1 16. The method according to ~~any of claims~~ 1 to 15, wherein a population
2 of tumor cells is transduced with a plurality of species of amplicons containing the genes for
3 the immunomodulatory protein and the additional therapeutic gene.

1 17. The method according to ~~any of claims~~ 1 to 16, wherein the
2 additional therapeutic gene encodes a second immunomodulatory protein.

1 18. The method according to ~~any of claims~~ 17, wherein the tumor cells
2 are transduced with amplicons encoding and expressing at least two species of cytokines.

1 19. The method according to claim 18, wherein tumor cells are
2 transduced with amplicons containing the genes for interleukin-2 and interleukin-12.

1 20. The method according to claim 18, wherein the tumor cells are
2 transduced with amplicons encoding and expressing a cytokine and a costimulatory factor.

1 21. The method according to claim 20, wherein tumor cells are
2 transduced with amplicons containing the genes for RANTES and B7.1.

1 22. The method according to any of claims 1-21, wherein the tumor cells
2 are hepatoma cells or lymphoma cells.

1 23. A mixture containing a plurality of species of herpes simplex virus
2 amplicons, including at least a first species of amplicon containing the gene for at least one
3 immunomodulatory protein and a second species of amplicon containing the gene for an
4 additional therapeutic gene product.

1 24. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a cytokine.

1 25. The mixture according to claim 24, wherein the cytokine is
2 interleukin-2 or granulocyte macrophage colony stimulating factor.

1 26. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a chemokine.

1 27. The mixture according to claim 26, wherein the chemokine is
2 RANTES.

1 28. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a intercellular adhesion molecule.

1 29. The mixture according to claim 28, wherein the intracellular adhesion
2 molecule is ICAM-1.

1 30. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a costimulatory factor.

1 31. The mixture according to claim 30, wherein the costimulatory factor
2 is B7.1.

1 *File C1* 32. The mixture according to ~~any of claims~~ claim 23 ~~-31~~, wherein the
2 additional therapeutic gene encodes a second immunomodulatory protein.

1 33. The mixture according to ~~any of claims~~ claim 23 ~~-32~~, wherein the
2 first and second species of amplicons contains genes encoding for RANTES and B7.1.

1 34. The mixture according to ~~any of claims~~ claim 23 ~~-32~~, wherein the
2 first and second species of amplicons contains genes encoding for at least two species of
3 cytokines.

1 35. The mixture according to claim 34, wherein the amplicons contain
2 genes encoding for interleukin-2 and interleukin-12.

1 36. Tumor cells transduced in accordance with the methods of ~~any of~~
2 *claims 1 to 22.*

1 37. Tumor cells transduced with a mixture of herpes simplex virus
2 *amplicons in accordance with any of claims 23 to 35.*

1 *File C1* 38. A method for production of an autologous vaccine to tumor cells
2 comprising transducing the tumor cells with a herpes simplex virus amplicon containing the
3 gene for an immunomodulatory protein to provide transient expression of the
4 immunomodulatory protein by the cells, wherein the immunomodulatory protein is selected
5 from among chemokines, intercellular adhesion molecules and costimulatory factors.

1 39. The method according to claim 1, wherein the tumor cells are
2 transduced with the herpes simplex amplicons *ex vivo.*

1 40. The method according to claim 1, wherein the tumor cells are
2 transduced with the herpes simplex cell *in vivo.*